DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-18) and the species psoriasis (disorder), tretinoin (retinoid), and misoprostol (prostaglandin) in the reply filed on 03/17/2008 is acknowledged.

Claims 6, 13, and 19-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the r

Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7-12, and 14-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for suppressing TNFα secretion, does not reasonably provide enablement for a method for treating a patient who has an immunoinflammatory disorder or a proliferative skin disease comprising administering a retinoid and a prostaglandin and it is not clear that a reasonably representative set of species of a retinoid and a prostaglandin would

be enabled for the treatment of such disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

To be enabling, the specification of the patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors. These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. In re Fisher, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill level:

It is unpredictable whether a drug can be used to treat a patient having a proliferative skin disease, such as cancer. In the case of cancer, it cannot be predicted if a drug will be successful in treating one type of cancer and this unpredictability increases when trying to treat a broad spectrum of cancers. Although many of the tests are functions related to cancers, these functions are not related to all cancers. Furthermore, even testing functions that are related to particular cancers can be misleading because a controlled environment in vitro cannot predict what will happen in vivo.

a. *Anticancer Assays*

The unpredictable nature of cancer assays has long been recognized. See, e.g., Gura (Science, vol. 278, pp. 1041-1042 (1997)), which provides an overview of the problems involved with sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile. Since formal screening began in 1955 many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (second paragraph of the article). As noted therein, the "fundamental problem in drug discovery for cancer is that the model systems are not predictive at all." The reasons are many, including basic differences between human patients on the one hand, and animal and cell culture models on the other (third paragraph of the article).

An efficient means of predicting activity with in vivo models remains desirable for compounds with anti-proliferative activity in vitro to this day. See the abstract of Johnson et al., British Journal of Cancer, vol. 84(10), pp. 1424-1431 (2001). As noted at the bottom of page 1424, the current "drug screening and development scheme remains an empirical one." See also the first paragraph of the "Discussion" section at page 1430 wherein the authors state that "analysis of xenograft versus clinical results illustrates that a histology to histology comparison of these models to activity in the clinic cannot be reliably discerned for these 'empirically' selected compounds acting against non-molecularly characterized tumors."

b. *Angiogenesis/Metastasis*

Therapies targeted to the common mechanism of angiogenesis have been tried as a means to overcoming the problems arising from the tremendous heterogeneity among different cancer types. Antiangiogenic therapies remain unpredictable, however, and have mainly failed due to numerous factors, including poor correlation between activity in rodent models and therapeutic efficacy in human patients; the tissue and/or tumor specific nature of vasculature; and the lack of a feasible means to monitor antiangiogenic response in patients. Due to these difficulties, additional markers associated with specific pathologies must further be identified, and even when there are no reasonable expectation of therapeutic success can be guaranteed (in part because drug delivery to the ischaemic site can be a major limiting factor, especially given the lack of tools

with which to monitor site specific drug availability within the tumor). See Gupta et al., Postgrad. Med. J., vol. 81, pp. 236-242 (2005) at the passage bridging the bottom of the left-hand column to the penultimate line on page 239.

As a result of such difficulties, different types of cancers must follow individualized strategies for angiogenesis based treatment. Consequently, most "treatments hold promise but will have to be clinically tested for different kinds and different stages of tumor growth." Gupta et al. at the left-hand column of page 240.

2. **The breadth of the claims:**

The claim is very broad and inclusive of the treatment of immunoinflammatory disorders and proliferative skin diseases, generally.

3. **The amount of direction or guidance provided and the presence or absence of working examples:**

The specification provides guidance for suppressing TNFα secretion. There is no guidance for the treatment of immunoinflammatory disorders and proliferative skin diseases, generally.

4. **The quantity of experimentation necessary:**

Because of the known unpredictability of the art, and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the instantly claimed method could be predictably used for the treatment of

immunoinflammatory disorders and proliferative skin diseases, generally, as inferred by the claim and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement requirement of §112, since to practice the invention claimed in the patent a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 112 – 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites the limitation "said inflammatory dermatosis" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 1-5, 7-12, and 14-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation, "**at risk** for developing an immunoinflammatory disorder or a proliferative skin disease". However, there is no guidance in the specification that clearly outlines who is or how to determine

who is "at risk" of developing the disorder or disease. Generally, anyone is "at risk" of developing an immunoinflammatory disorder or a proliferative skin disease (e.g., acne).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a

later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7-12, and 14-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2001/0053764 in view of Frost et al. (JAMA, March 10, 1969; 207(10):1863-1868).

US 2001/0053764 discloses methods of treating psoriatic lesions that involve administering to a human patient a therapeutically effective amount of a soluble type II IL-1 receptor. The treatment is effective against psoriatic lesions that occur in patients who have ordinary psoriasis or psoriatic arthritis (¶ [0064]). Soluble type II IL-1 receptor may be used to treat ordinary psoriasis in combination with one, two, three or more other medications that are effective against psoriasis. These additional medications may be administered before, simultaneously with, or sequentially with the soluble type II IL-1 receptor (¶ [0068]). The soluble type II IL-1 receptor may be used to treat psoriasis in combination with misoprostol and other drugs that may treat psoriasis (¶ [0069]). Any efficacious route of administration may be used including topically (e.g., topical preparations such as lotions, gels, etc.) [¶ [0020]). The reference does not expressly teach the combination therapy of an immunoinflammatory disorder or a proliferative skin disease using a prostaglandin and a retinoid.

Frost et al teach that 0.1 to 0.3% topically administered vitamin A acid (i.e., tretinoin) applied twice daily (page 1865, first column, first full paragraph) is

effective in treating psoriasis (abstract; page 1863, first column bridging to second column). The reference does not expressly teach the combination therapy of an immunoinflammatory disorder or a proliferative skin disease using a prostaglandin and a retinoid.

The skilled artisan would have found it obvious at the time of the invention to use a prostaglandin and a retinoid together to treat an immunoinflammatory disorder or a proliferative skin disease.

The artisan would have been motivated by the reasonable expectation of successfully treating psoriasis by topically administering a composition comprising misoprostol and tretinoin. Generally, it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in the prior art. In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980): In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960). Conversely, there is no evidence in the record establishing the Applicant's combination of agents is any more effective or in any way different than any single member of that combination. See In re Dial, 140 USPQ 244 (C.C.P.A. 1964).

As for the amounts to be administered per day, it is commonly practiced in pharmaceutical treatment of diseases to alter the amount of drug to be administered depending on different factors such as the severity of the disease.

Conclusion

No claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRIS E. SIMMONS whose telephone number is (571)272-9065. The examiner can normally be reached on Monday - Friday from 7:30 - 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Chris E Simmons/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612